Complete Summary

GUIDELINE TITLE

Guidelines for the diagnosis and treatment of non-ST-segment elevation acute coronary syndromes.

BIBLIOGRAPHIC SOURCE(S)

Bassand JP, Hamm CW, Ardissino D, Boersma E, Budaj A, Fernandez-Aviles F, Fox KA, Hasdai D, Ohman EM, Wallentin L, Wijns W, ESC Committee for Practice Guidelines (CPG), Vahanian A, Camm J, De Caterina R, Dean V, Dickstein K, Filippatos G, Kristensen SD, Widimsky P, McGregor K, Sechtem U, Tendera M, Hellemans I, Gomez JL, Silber S, Funck-Brentano C, Kristensen SD, Andreotti F, Benzer W, Bertrand M, Betriu A, De Caterina R, DeSutter J, Falk V, Ortiz AF, Gitt A, Hasin Y, Huber K, Kornowski R, Lopez-Sendon J, Morais J, Nordrehaug JE, Silber S, Steg PG, Thygesen K, Tubaro M, Turpie AG, Verheugt F, Windecker S, Task Force for Diagnosis and Treatment of Non-ST-Segment Elevation Acute. Guidelines for the diagnosis and treatment of non-ST-segment elevation acute coronary syndromes. The Task Force for the Diagnosis and Treatment of Non-ST-Segment Elevation Acute Coronary Syndromes of the European Society of Cardiology. Eur Heart J 2007 Jul;28(13):1598-660. [514 references] PubMed

GUIDELINE STATUS

This is the current release of the guideline.

This guideline updates a previous version: Bertrand ME, Simoons ML, Fox KA, Wallentin LC, Hamm CW, McFadden E, De Feyter PJ, Specchia G, Ruzyllo W. Management of acute coronary syndromes in patients presenting without persistent ST-segment elevation. Eur Heart J 2002 Dec;23(23):1809-40.

**** REGULATORY ALERT ****

FDA WARNING/REGULATORY ALERT

Note from the National Guideline Clearinghouse: This guideline references a drug(s) for which important revised regulatory and/or warning information has been released.

- February 28, 2008, Heparin Sodium Injection: The U.S. Food and Drug Administration (FDA) informed the public that Baxter Healthcare Corporation has voluntarily recalled all of their multi-dose and single-use vials of heparin sodium for injection and their heparin lock flush solutions. Alternate heparin manufacturers are expected to be able to increase heparin production sufficiently to supply the U.S. market. There have been reports of serious adverse events including allergic or hypersensitivity-type reactions, with

symptoms of oral swelling, nausea, vomiting, sweating, shortness of breath, and cases of severe hypotension.

- June 8, 2007, Troponin-I Immunoassay: Class I Recall of all lots of the Architect Stat Troponin-I Immunoassay. The assay may report falsely elevated or falsely decreased results at and near a low level, which may impact patient treatment.

COMPLETE SUMMARY CONTENT

** REGULATORY ALERT **
SCOPE
METHODOLOGY - including Rating Scheme and Cost Analysis
RECOMMENDATIONS
EVIDENCE SUPPORTING THE RECOMMENDATIONS
BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS
CONTRAINDICATIONS
QUALIFYING STATEMENTS
IMPLEMENTATION OF THE GUIDELINE
INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES
IDENTIFYING INFORMATION AND AVAILABILITY
DISCLAIMER

SCOPE

DISEASE/CONDITION(S)

Acute coronary syndromes without persistent ST-segment elevation

GUIDELINE CATEGORY

Diagnosis
Evaluation
Management
Risk Assessment
Treatment

CLINICAL SPECIALTY

Cardiology
Emergency Medicine

INTENDED USERS

Advanced Practice Nurses
Nurses
Physician Assistants
Physicians

GUIDELINE OBJECTIVE(S)

To present recommendations on the management of patients with suspected acute coronary syndromes without persistent ST-segment elevation

TARGET POPULATION

Patients with suspected acute coronary syndromes without persistent ST-segment elevation

INTERVENTIONS AND PRACTICES CONSIDERED

Diagnosis, Risk Assessment

1. Electrocardiogram
2. Laboratory examinations
3. Measurement of biomarkers of cardiac damage (cardiac troponin or tropinin I)
4. Risk score assessment
5. Echocardiogram
6. Stress test

Treatment

1. Anti-ischaemic agents, such as beta-blockers; nitrates; and calcium channel blockers
2. Anticoagulants, such as unfractionated heparin; low-molecular-weight heparins, factor Xa inhibitors, direct thrombin inhibitors, and vitamin K antagonists.
3. Antiplatelet agents, such as aspirin; adenosine diphosphate receptor antagonists; and glycoprotein IIb/IIIa receptor blockers
4. Coronary revascularization procedures
    - Coronary angiography
    - Percutaneous coronary interventions, such as balloon angioplasty, stent implantation
    - Coronary artery bypass surgery
    - Percutaneous coronary interventions and surgery

Long-Term Management

1. Risk factor modification
2. Long-term treatment with aspirin
3. Long-term beta-blocker therapy
4. Smoking cessation
5. Lipid-lowering therapy (statins)
6. Angiotensin-converting enzyme (ACE) inhibitors
7. Angiotensin receptor blockers
8. Aldosterone receptor antagonists
9. Rehabilitation (assessment of functional capacity, resumption of normal activity)
10. Management of complications (e.g., thrombocytopenia)
11. Management of special patient populations (elderly, women, patients with diabetes, patients with chronic kidney disease, patients with anaemia

MAJOR OUTCOMES CONSIDERED

- Prognostic value of diagnostic tests
- Death (mortality) rates
- Myocardial infarction rates
- Incidence of angina
- Thrombosis formation
- Symptom relief
- Recurrent or ongoing myocardial ischaemia/infarction

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Searches were performed of the following resources: PubMed, medical journals by speciality, the Cochrane Library.

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Levels of Evidence

Level of Evidence A: Data derived from multiple randomized clinical trials or meta-analyses

Level of Evidence B: Data derived from a single randomized clinical trial or large non-randomized studies

Level of Evidence C: Consensus of opinion of the experts and/or small studies, retrospective studies, registries

METHODS USED TO ANALYZE THE EVIDENCE

Review of Published Meta-Analyses
Systematic Review with Evidence Tables

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

Not stated

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Classes of Recommendations

Class I = Evidence and/or general agreement that a given treatment is beneficial, useful and effective

Class II = Conflicting evidence and/or a divergence of opinion about the usefulness/efficacy of the given treatment or procedure

IIa: Weight of evidence/opinion is in favour of usefulness/efficacy

IIb: Usefulness/efficacy is less well established by evidence/opinion

Class III = Evidence or general agreement that the given treatment or procedure is not useful/effective and in some cases may be harmful.

COST ANALYSIS

The guideline developers reviewed published cost analyses.

METHOD OF GUIDELINE VALIDATION

External Peer Review
Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Once the document has been finalized and approved by all the experts involved in the Task Force, it is submitted to outside specialists for review. The document is revised, and finally approved by the European Society of Cardiology (ESC) Committee for Practice Guidelines and subsequently published.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Definitions for the classes of recommendations (I-III) and the levels of evidence (A-C) can be found at the end of the "Major Recommendations" field.

Diagnosis and Risk Stratification

- Diagnosis and short-term risk stratification of Non-ST-Segment Elevation Acute Coronary Syndrome (NSTE-ACS) should be based on a combination of clinical history, symptoms, electrocardiogram (ECG), biomarkers, and risk score results **(I-B)**.
- The evaluation of the individual risk is a dynamic process that is to be updated as the clinical situation evolves.
    - A 12-lead ECG should be obtained within 10 min after first medical contact and immediately read by an experienced physician **(I-C)**. Additional leads (V_3R and V_4R, V_7–V_9) should be recorded. ECG should be repeated in the case of recurrence of symptoms, and at 6 and 24 hours and before hospital discharge **(I-C)**.
    - Blood must be drawn promptly for troponin (cTnT or cTnI) measurement. The result should be available within 60 minutes **(I-C)**. The test should be repeated after 6 to 12 hours if the initial test is negative **(I-A)**.
    - Established risk scores (such as global registry of acute coronary events [GRACE]) should be implemented for initial and subsequent risk assessment **(I-B)**.
    - An echocardiogram is recommended to rule in/out differential diagnoses **(I-C)**.
    - In patients without recurrence of pain, normal ECG findings, and negative troponins tests, a non-invasive stress test for inducible ischaemia is recommended before discharge **(I-A)**.
- The following predictors of long-term death or myocardial infarction (MI) should be considered in risk stratification **(I-B)**.
    - Clinical indicators: age, heart rate, blood pressure, Killip class, diabetes, previous myocardial infarction (MI)/ coronary artery disease (CAD)
    - ECG markers: ST-segment depression
    - Laboratory markers: troponins, glomerular filtration rate (GFR)/ creatinine clearance (CrCl)/cystatin C, plasma B-type natriuretic peptide (BNP)/ N-terminal prohormone brain natriuretic peptide (NT-proBNP), high sensitive C-reactive protein (hsCRP)
    - Imaging findings: low ejection fraction (EF), main stem lesion, three vessel disease
    - Risk score result

Treatment

Recommendations for Anti-ischaemic Drugs

- Beta-blockers are recommended in the absence of contraindications, particularly in patients with hypertension or tachycardia **(I-B)**.
- Intravenous or oral nitrates are effective for symptom relief in the acute management of anginal episodes **(I-C)**.
- Calcium channel blockers provide symptom relief in patients already receiving nitrates and beta-blockers; they are useful in patients with contraindications to beta-blockade and in the subgroup of patients with vasospastic angina **(I-B)**.

- Nifedipine, or other dihydropyridines, should not be used unless combined with beta-blockers **(III-B)**.

Recommendations for Anticoagulation

- Anticoagulation is recommended for all patients in addition to antiplatelet therapy **(I-A)**.
- Anticoagulation should be selected according to the risk of both ischaemic and bleeding events **(I-B)** (see section on 6.1, Bleeding complications; section 7.4, Chronic kidney disease; and section 7.5, Anaemia, in the original guideline document).
- Several anticoagulants are available, namely unfractionated heparin (UFH), Low molecular weight heparin (LMWH), fondaparinux, and bivalirudin. The choice depends on the initial strategy (see section 8, Management strategies: urgent invasive, early invasive, or conservative strategies in the original guideline document) **(I-B)**.
- In an urgent invasive strategy, UFH **(I-C)**, enoxaparin **(IIa-B)**, or bivalirudin **(I-B)** should be immediately started.
- In an non-urgent situation, as long as a decision between an early invasive or conservative strategy is pending (see section 8, Management strategies in the original guideline document):
    - Fondaparinux is recommended on the basis of the most favourable efficacy/safety profile **(I-A)** (see sections 5.2.3, Factor-Xa inhibitors and 6.1, Bleeding complications in the original guideline document).
    - Enoxaparin with a less favourable efficacy/safety profile than fondaparinux should be used only if the bleeding risk is low **(IIa-B)**.
    - As the efficacy/safety profile of LMWH (other than enoxaparin) or UFH relative to fondaparinux is unknown, these anticoagulants cannot be recommended over fondaparinux **(IIa-B)**.
    - At percutaneous coronary intervention (PCI) procedures, the initial anticoagulant should also be maintained during the procedure regardless of whether this treatment is UFH **(I-C)**, enoxaparin **(IIa-B)**, or bivalirudin **(I-B)**, whereas additional UFH in standard dose (50 to 100 IU/kg bolus) is necessary in the case of fondaparinux **(IIa-C)**.
    - Anticoagulation can be stopped within 24 hours after an invasive procedure **(IIa-C)**. In a conservative strategy, fondaparinux, enoxaparin, or other LMWH may be maintained up to hospital discharge **(I-B)**.

Recommendations for Oral Antiplatelet Drugs

(See Table 6 in the original guideline document for dosing information)

- Aspirin is recommended for all patients presenting with NSTE-ACS without contraindication at an initial loading dose of 160 to 325 mg (non-enteric) **(I-A)**, and at a maintenance dose of 75 to 100 mg long-term **(I-A)**.
- For all patients, an immediate 300 mg loading dose of clopidogrel is recommended, followed by 75 mg clopidogrel daily **(I-A)**. Clopidogrel should be maintained for 12 months unless there is an excessive risk of bleeding **(I-A)**.
- For all patients with contraindication to aspirin, clopidogrel should be given instead **(I-B)**.

- In patients considered for an invasive procedure/PCI, a loading dose of 600 mg of clopidogrel may be used to achieve more rapid inhibition of platelet function **(IIa-B)**.
- In patients pre-treated with clopidogrel who need to undergo CABG, surgery should be postponed for 5 days for clopidogrel withdrawal if clinically feasible **(IIa-C)**.

Recommendations for Glycoprotein IIb/IIa Inhibitors

(See Table 6 in the original guideline document for dosing information)

- In patients at intermediate to high risk, particularly patients with elevated troponins, ST-depression, or diabetes, either eptifibatide or tirofiban for initial early treatment is recommended in addition to oral antiplatelet agents **(IIa-A)**.
- The choice of combination of antiplatelet agents and anticoagulants should be made in relation to risk of ischaemic and bleeding events **(I-B)**.
- Patients who receive initial treatment with eptifibatide or tirofiban prior to angiography should be maintained on the same drug during and after PCI **(IIa-B)**.
- In high-risk patients not pre-treated with glycoprotein (GP) IIb/IIIa inhibitors and proceeding to PCI, abciximab is recommended immediately following angiography **(I-A)**. The use of eptifibatide or tirofiban in this setting is less well established **(IIa-B)**.
- GP IIb/IIIa inhibitors must be combined with an anticoagulant **(I-A)**.
- Bivalirudin may be used as an alternative to GP IIb/IIIa inhibitors plus UFH/LMWH **(IIa-B)**.
- When anatomy is known and PCI planned to be performed within 24 hours with GP IIb/IIIa inhibitors, most secure evidence is for abciximab **(IIa-B)**.

Recommendations for Resistance to Antiplatelet Treatment/ Drug Interactions

- Routine assessment of platelet aggregation inhibition in patients submitted to either aspirin or clopidogrel therapy, or both, is not recommended **(IIb-C)**.
- Nonsteroidal anti-inflammatory drugs (NSAIDs) (selective COX-2 inhibitors and non-selective NSAIDs) should not be administered in combination with either aspirin or clopidogrel **(III-C)**.
- Clopidogrel can be administered with all statins **(I-B)**.
- The triple association of aspirin, clopidogrel, and a Vitamin K antagonist (VKA) should only be given if a compelling indication exists, in which case, the lowest efficacious international normalized ratio (INR) and shortest duration for the triple association should be targeted **(IIa-C)**.

Recommendations for Withdrawal of Antiplatelet Treatment

- Temporary interruption of dual antiplatelet therapy (aspirin and clopidogrel) within the first 12 months after the initial episode is discouraged **(I-C)**.
- Temporary interruption for major or life-threatening bleeding or for surgical procedures where even minor bleeding may result in severe consequences (brain or spinal surgery) is mandatory **(IIa-C)**.

- Prolonged or permanent withdrawal of aspirin, clopidogrel, or both is discouraged unless clinically indicated. Consideration should be given to the risk of recurrence of ischaemic events which depends (among other factors) on initial risk, on the presence and type of stent implanted, and on the time window between proposed withdrawal and the index event and/or revascularization **(I-C)**.

Recommendations for Invasive Evaluation and Revascularization

(See also section 8, Management strategies in the original guideline document).

- Urgent coronary angiography is recommended in patients with refractory or recurrent angina associated with dynamic ST-deviation, heart failure, life threatening arrhythmias, or haemodynamic instability **(I-C)**.
- Early (<72 h) coronary angiography followed by revascularization (PCI or coronary artery bypass grafting [CABG]) in patients with intermediate to high-risk features is recommended **(I-A)**.
- Routine invasive evaluation of patients without intermediate to high-risk features is not recommended **(III-C)**, but non-invasive assessment of inducible ischaemia is advised **(I-C)**.
- PCI of non-significant lesions is not recommended **(III-C)**.
- After critical evaluation of the risk–benefit ratio, and depending on known co-morbidities and potential need for non-cardiac surgery in the short/medium term (e.g. planned intervention or other conditions) requiring temporary withdrawal of dual antiplatelet therapy, consideration should be given to the type of stent to be implanted (Bristol-Myers Squibb [BMS] or drug eluding stents [DES]) **(I-C)**.

Recommendations for Lipid-lowering Therapy

- Statins are recommended for all NSTE-ACS patients (in the absence of contraindications), irrespective of cholesterol levels, initiated early (within 1 to 4 days) after admission, with the aim of achieving low density lipoprotein cholesterol (LDLc) levels <100 mg/dL (<2.6 mmol/L) **(I-B)**.
- Intensive lipid-lowering therapy with target LDLc levels <70 mg/dL (<1.81 mmol/L) initiated within 10 days after admission is advisable **(IIa-B)**.

Recommendations for use of Beta-Blockers

- Beta-blockers should be given to all patients with reduced left ventricle (LV) function **(I-A)**.

Recommendations for the use of Angiotensin-Converting Enzyme (ACE) Inhibitors

- ACE inhibitors are indicated long-term in all patients with left ventricular ejection fraction (LVEF) $\leq$40% and in patients with diabetes, hypertension, or chronic kidney disease (CKD), unless contraindicated **(I-A)**.
- ACE inhibitors should be considered for all other patients to prevent recurrence of ischaemic events **(IIa-B)**. Agents and doses of proven efficacy are recommended **(IIa-C)**.

Recommendations for the use of Angiotensin Receptor Blockers (ARBs)

- ARBs should be considered in patients who are intolerant to ACE inhibitors and/or who have heart failure or MI with LVEF <40% **(I-B)**.

Recommendations for Aldosterone Receptor Antagonists

- Aldosterone blockade should be considered in patients after MI who are already treated with ACE inhibitors and beta-blockers and who have an LVEF <40% and either diabetes or heart failure, without significant renal dysfunction or hyperkalaemia **(I-B)**.

Recommendations for Rehabilitation and Return to Physical Activity

- After NSTE-ACS, assessment of functional capacity is recommended **(I-C)**.
- Every patient after NSTE-ACS should undergo an ECG guided exercise test (if technically feasible) or an equivalent non-invasive test for ischaemia, within 4 to 7 weeks after discharge **(IIa-C)**.
- On the basis of cardiovascular status and the results of functional physical capacity assessment, patients should be informed about the timing of resumption and the recommended level of physical activity, including leisure, work, and sexual activities **(I-C)**.

<u>Complications and their Management</u>

Recommendations for Bleeding Complications

- Assessment of bleeding risk is an important component of the decision-making process. Bleeding risk is increased with higher or excessive doses of antithrombotic agents, length of treatment, combinations of several antithrombotic drugs, switch between different anticoagulant drugs, as well as with older age, reduced renal function, low body weight, female gender, baseline haemoglobin, and invasive procedures **(I-B)**.
- Bleeding risk should be taken into account when deciding on a treatment strategy. Drugs, combination of drugs, and non-pharmacological procedures (vascular access) known to carry a reduced risk of bleeding should be preferred in patients at high risk of bleeding **(I-B)**.
- Minor bleeding should preferably be managed without interruption of active treatments **(I-C)**.
- Major bleeding requires interruption and/or neutralization of both anticoagulant and antiplatelet therapy, unless bleeding can be adequately controlled by specific haemostatic intervention **(I-C)**.
- Blood transfusion may have deleterious effects on outcome and should therefore be considered individually, but withheld in haemodynamically stable patients with haematocrit >25% or haemoglobin level >8 g/L **(I-C)**.

Recommendations for Thrombocytopenia

- Significant thrombocytopenia (<100 000 microliters $^{(-1)}$ or >50% drop in platelet count) occurring during treatment with GP IIb/IIIa inhibitors and/or

heparin (LMWH or UFH) requires the immediate interruption of these drugs **(I-C)**.
- Severe thrombocytopenia (<10 000 microliters $^{(-1)}$) induced by GP IIb/IIIa inhibitors requires platelet transfusion with or without fibrinogen supplementation with fresh–frozen plasma or cryoprecipitate in the case of bleeding **(I-C)**.
- Interruption of heparin (UFH or LMWH) is warranted in the case of documented or suspected heparin-induced thrombocytopenia (HIT). In the case of thrombotic complications, anticoagulation can be achieved with a direct thrombin inhibitor (DTI) **(I-C)**.
- Prevention of HIT can be achieved with the use of anticoagulants devoid of risk of HIT, such as fondaparinux or bivalirudin, or by brief prescription of heparin (UFH or LMWH) in cases where these compounds are chosen as anticoagulant **(I-B)**.

Special Populations and Conditions

Recommendations for the Elderly

- Elderly patients (>75 years old) often have atypical symptoms. Active screening for NSTE-ACS should be initiated at lower levels of suspicion than among younger (<75 years old) patients **(I-C)**.
- Treatment decisions in the elderly should be tailored according to estimated life expectancy, patient wishes, and co-morbidities to minimize risk and improve morbidity and mortality outcomes in this frail but high-risk population **(I-C)**.
- Elderly patients should be considered for routine early invasive strategy, after careful evaluation of their inherent raised risk of procedure-related complications, especially during CABG **(I-B)**.

Recommendations for Women

- Women should be evaluated and treated in the same way as men, with special attention to co-morbidities **(I-B)**.

Recommendations for Diabetes

- Tight glycaemic control to achieve normoglycaemia as soon as possible is recommended in all diabetic patients with NSTE-ACS in the acute phase **(I-C)**.
- Insulin infusion may be needed to achieve normoglycaemia in selected NSTE-ACS patients with high blood glucose levels at admission **(IIa-C)**.
- An early invasive strategy is recommended for diabetic patients with NSTE-ACS **(I-A)**.
- Diabetic patients with NSTE-ACS should receive intravenous GP IIb/IIIa inhibitors as part of the initial medical management which should be continued through the completion of PCI **(IIa-B)**.

Recommendations for Patients with CKD

- Creatinine clearance (CrCl) and/or GFR should be calculated for every patient hospitalized for NSTE-ACS **(I-B)**. Elderly people, women, and low body weight patients merit special attention as near normal serum creatinine levels may be associated with lower than expected CrCl and GFR levels **(I-B)**.
- Patients with CKD should receive the same first-line treatment as any other patient, in the absence of contraindications **(I-B)**.
- In patients with CrCl <30 mL/min or GFR <30 mL/min/ 1.73 m^2, a careful approach to the use of anticoagulants is recommended, since dose adjustment is necessary with some, while others are contraindicated **(I-C)**.
- UFH infusion adjusted according to activated partial thromboplastin time (aPTT) is recommended when CrCl <30 mL/min or GFR <30 mL/min/1.73 m^2 **(I-C)**.
- GP IIb/IIIa inhibitors can be used in the case of renal failure. Dose adaptation is needed with eptifibatide and tirofiban. Careful evaluation of the bleeding risk is recommended for abciximab **(I-B)**.
- Patients with CKD with CrCl <60 mL/min are at high risk of further ischaemic events and therefore should be submitted to invasive evaluation and revascularization whenever possible **(IIa-B)**.
- Appropriate measures are advised in order to reduce the risk of contrast-induced nephropathy (CIN) **(I-B)**.

Recommendations for Anaemia

- Low baseline haemoglobin is an independent marker of the risk of ischaemic and bleeding events at 30 days. It should be taken into consideration in assessing initial risk **(I-B)**.
- All necessary measures should be taken during the course of initial management to avoid worsening of anaemia by bleeding **(I-B)** (see section 6.1, Bleeding complications in the original guideline document).
- Well-tolerated anaemia at baseline in patients with NSTE-ACS should not lead to systematic blood transfusion which should be considered only in the case of compromised haemodynamic status **(I-C)** (see section 6.1, Bleeding complications in the original guideline document).

Management Strategies

Recommendations for Performance Measures

- Development of regional and/or national programmes to measure performance indicators systematically and provide feedback to individual hospitals is strongly encouraged **(I-C)**.

Definitions:

Levels of Evidence

Level of Evidence A: Data derived from multiple randomized clinical trials or meta-analyses

Level of Evidence B: Data derived from a single randomized clinical trial or large non-randomized studies

Level of Evidence C: Consensus of opinion of the experts and/or small studies, retrospective studies, registries

Classes of Recommendations

Class I = Evidence and/or general agreement that a given treatment is beneficial, useful and effective

Class II = Conflicting evidence and/or a divergence of opinion about the usefulness/efficacy of the given treatment or procedure

IIa: Weight of evidence/opinion is in favour of usefulness/efficacy

IIb: Usefulness/efficacy is less well established by evidence/opinion

Class III = Evidence or general agreement that the given treatment or procedure is not useful/effective and in some cases may be harmful.

CLINICAL ALGORITHM(S)

An algorithm is provided in the original guideline document titled "Decision-making algorithm for the management of patients with non ST-elevation acute coronary syndrome."

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is identified and graded for selected recommendations (see "Major Recommendations").

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Appropriate management of patients with non-ST-segment elevation acute coronary syndromes that may help to improve both immediate and long-term outcomes

POTENTIAL HARMS

Nitrates

- Side effects include headache and hypotension.

Calcium Channel Blockers

- Atrioventricular (A-V) block may be induced by non-dihydropyridines

- Several analyses of pooled data from observational studies suggest that short-acting nifedipine might be associated with a dose-dependent detrimental effect on mortality in patients with coronary artery disease.

Antithrombin Drugs

- Antithrombotic agents may cause bleeding complications
- Heparin can induce thrombocytopenia.

Aspirin

- The most common side effect of aspirin is gastrointestinal intolerance. Gastrointestinal bleeding appears to increase with high doses. Aspirin can induce respiratory tract disease, rash, and skin manifestations. Hypersensitivity and anaphylactic shock can occur but are rare.

Clopidogrel

- An increase in the rate of major bleeding was observed in clopidogrel-treated patients.

Glycoprotein IIb/IIIa Inhibitors

- Bleeding, haematoma, and thrombocytopenia can occur with this class of drugs. Bleeding risk is clearly related to the dose of adjunctive heparin and specific reduced dosing schedules are recommended.

Subgroups Most Likely to be Harmed

- Patients with significantly impaired atrioventricular conduction and a history of asthma or of acute left ventricular dysfunction should not receive beta-blockers.
- Excessive doses of drugs, especially in women, elderly patients, or those with renal failure, also increase the risk of bleeding.

CONTRAINDICATIONS

CONTRAINDICATIONS

- Beta-blockers are contraindicated in patients with significantly impaired atrioventricular conduction, a history of asthma, or of acute left ventricular dysfunction.
- Nitric oxide donor therapy (nitrates and sydnonimines) is contraindicated in patients taking phosphodiesterase-5 inhibitors (sildenafil, vardenafil, tadalafil) because of the risk of profound vasodilatation and blood pressure drop in the case of concomitant administration
- Pre-treatment with a triple or even dual antiplatelet regimen should be considered as only a relative contraindication to early coronary artery bypass surgery

- In case of severe renal failure (creatinine clearance (CrCl) <30 mL/min), many drugs with exclusive or substantial renal elimination need to be down-titrated or might even be contraindicated, particularly low molecular weight heparin (LMWH), fondaparinux, bivalirudin and glycoprotein (GP) IIb/IIIa inhibitors.
- Angiotensin converting enzyme (ACE) inhibitors are contraindicated in patients with renal artery stenosis

Refer to Table 10 in the original guideline document for more contraindications of drugs used for chronic kidney disease.

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

The European Society of Cardiology (ESC) Guidelines represent the views of the ESC and were arrived at after careful consideration of the available evidence at the time they were written. Health professionals are encouraged to take them fully into account when exercising their clinical judgment. The guidelines do not, however, override the individual responsibility of health professionals to make appropriate decisions in the circumstances of the individual patients, in consultation with that patient, and where appropriate and necessary the patient's guardian or carer. It is also the health professional's responsibility to verify the rules and regulations applicable to drugs and devices at the time of prescription.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

IMPLEMENTATION TOOLS

Clinical Algorithm
Personal Digital Assistant (PDA) Downloads
Pocket Guide/Reference Cards
Slide Presentation

For information about availability, see the "Availability of Companion Documents" and "Patient Resources" fields below.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Getting Better
Living with Illness

IOM DOMAIN

Effectiveness
Patient-centeredness
Timeliness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Bassand JP, Hamm CW, Ardissino D, Boersma E, Budaj A, Fernandez-Aviles F, Fox KA, Hasdai D, Ohman EM, Wallentin L, Wijns W, ESC Committee for Practice Guidelines (CPG), Vahanian A, Camm J, De Caterina R, Dean V, Dickstein K, Filippatos G, Kristensen SD, Widimsky P, McGregor K, Sechtem U, Tendera M, Hellemans I, Gomez JL, Silber S, Funck-Brentano C, Kristensen SD, Andreotti F, Benzer W, Bertrand M, Betriu A, De Caterina R, DeSutter J, Falk V, Ortiz AF, Gitt A, Hasin Y, Huber K, Kornowski R, Lopez-Sendon J, Morais J, Nordrehaug JE, Silber S, Steg PG, Thygesen K, Tubaro M, Turpie AG, Verheugt F, Windecker S, Task Force for Diagnosis and Treatment of Non-ST-Segment Elevation Acute. Guidelines for the diagnosis and treatment of non-ST-segment elevation acute coronary syndromes. The Task Force for the Diagnosis and Treatment of Non-ST-Segment Elevation Acute Coronary Syndromes of the European Society of Cardiology. Eur Heart J 2007 Jul;28(13):1598-660. [514 references] PubMed

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2000 Sep (revised 2007)

GUIDELINE DEVELOPER(S)

European Society of Cardiology - Medical Specialty Society

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Task Force for the Diagnosis and Treatment of Non-ST-Segment Elevation Acute Coronary Syndromes

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The experts of the writing panels have provided disclosure statements of all relationships they may have which might be perceived as real or potential sources of conflicts of interest. These disclosure forms are kept on file at the European Heart House, headquarters of the European Society of Cardiology (ESC). Any changes in conflict of interest that arise during the writing period must be notified to the ESC.

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GUIDELINE STATUS

This is the current release of the guideline.

This guideline updates a previous version: Bertrand ME, Simoons ML, Fox KA, Wallentin LC, Hamm CW, McFadden E, De Feyter PJ, Specchia G, Ruzyllo W. Management of acute coronary syndromes in patients presenting without persistent ST-segment elevation. Eur Heart J 2002 Dec;23(23):1809-40.

GUIDELINE AVAILABILITY

Electronic copies: Available from the European Society of Cardiology (ESC) Web site.

Print copies: Available from Oxford University Press, Great Clarendon Street, Oxford, OX2 6DP, UK, Tel: +44 (0) 1865 353263, Fax: +44 (0) 1865 353774, Web site: http://www.eurheartj.oxfordjournals.org/.

AVAILABILITY OF COMPANION DOCUMENTS

The following are available:

- ESC guidelines for the management of non-ST segment elevation acute coronary syndromes. Slide set. Electronic copies: Available in Portable Document Format (PDF) from the European Society of Cardiology (ESC) Web site.
- Diagnosis and treatment of non-ST-segment elevation acute coronary syndromes. Pocket guideline. Electronic copies: Available from the European Society of Cardiology (ESC) Web site. Also available for PDA download from the ESC Web site.
- Recommendations for guidelines production. A document for Task Force Members responsible for the production and updating of ESC guidelines. 2006 Jun 28. 21 p. Available from the ESC Web site.

Print copies: Available from Oxford University Press, Great Clarendon Street, Oxford, OX2 6DP, UK, Tel: +44 (0) 1865 353263, Fax: +44 (0) 1865 353774, Web site: http://www.eurheartj.org/.

PATIENT RESOURCES

None available

NGC STATUS

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